REMARKS

Applicant thanks the Examiner for courtesies extended during the telephone interview of July 15, 2003.

In view of the amendments and remarks made herein, reconsideration and withdrawal of any rejections of the application, and allowance of the claims are respectfully requested.

I. STATUS OF THE CLAIMS

Claims 34-44 are pending in the application. Claims 1-33 have been canceled, and claims 34-44 added without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents. Support for new claims 34-44 is found throughout the specification, particularly in the original claims.

No new matter is added.

It is respectfully submitted that the claims herewith and the claims as originally presented are and were in full compliance with the requirements of 35 U.S.C. §§101, 102, 103 and 112. The amendments to these claims, and remarks concerning these claims, were not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112, but rather for clarification and to round out the scope of protection to which the Applicant is entitled.

II. THE §112 REJECTIONS ARE OVERCOME

Claim 19 was rejected under 35 U.S.C. §112, first paragraph. Claims 12 and 21-33 were rejected under 35 U.S.C. §112, second paragraph. In view of the cancellation of claims 1-33 and the addition of new claims 34-44, reconsideration and withdrawal of the rejections is requested. Specifically, and following the Examiner's helpful suggestion, claim 34 is drawn to a method for preventing the occurrence of gastric ulcers in a horse subject to a stress that causes gastric ulcers, and claim 38 depends from claim 34 and recites the stresses of training, transportation, change in environment, or pregnancy.

III. THE §103 REJECTIONS ARE OVERCOME

Claims 1-19 and 21-33 were rejected under 35 U.S.C. §103(a) as allegedly being rendered obvious by FDA Federal Register ("FDA"), Papich, or WO 96/31213, alone or in

combination. In view of the cancellation of claims 1-33 and the addition of new claims 34-44, reconsideration and withdrawal of the rejections is respectfully requested.

The Office Action (at 2) asserts that FDA relates to the use of omeprazole for the prevention of gastric ulcers in horses. As noted in the Amendment mailed on December 18, 2002 (at 5), FDA only pertains to the use of omeprazole for the treatment of gastric ulcers in horses and for the prevention of reoccurrence of gastric ulcers in horses. The July 30, 2003 Advisory Action asserts that the instant claims "do not exclude a horse who has had ulcers in the past." Applicant respectfully disagrees because the recitation of administering omeprazole "prior to occurrence of gastric ulcer conditions" in base independent claim 34 does not refer to conditions that cause ulcers, but instead refers to horses that have not previously had gastric ulcers (i.e., "gastric ulcer conditions").

The Office Action (at 3) asserts that Papich relates to the use of omeprazole for the prevention of gastric ulcers in small animals, including dogs. As noted in the Amendment mailed on December 18, 2002 (at 6), Papich only pertains to the use of omeprazole in small animals in cases where the animals are susceptible to the development of gastric ulcers because of concurrent disease or drug therapy. Papich principally relates to the treatment of NSAID-induced ulcers in dogs. Furthermore, there are profound differences between the gastrointestinal physiology of horses and that of small animals such as dogs. As discussed in the Horse Gastric Ulcer Bulletin from Tufts University School of Veterinary Medicine (www.tufts.edu/vet/sports/ulcers.html; "Tufts Bulletin;" Exhibit 1) and in Canine Nutrition (www.knowbetterdogfood.com/dogcare/health/nutrition.php; Exhibit 2), differences between horse and dog gastrointestinal physiology reflect differences between herbivore and carnivore specialization. The physiological mechanisms and anatomical specializations required to support cellulose digestion are markedly different from those needed for the digestion of meat. For example, the stomachs of horses are specialized for frequent small meals—i.e., relatively small and tonic gastric acid secreting (see Tufts Bulletin, at 1). Therefore, it is respectfully submitted that, in view of the differences between horse and dog digestive physiology and Papich's focus on NSAID-induced ulcers in dogs, a skilled artisan would not be motivated to modify Papich to arrive at the instantly claimed invention.

WO 96/31213 relates to compositions comprising proton-pump inhibitors.

In summary, new independent claim 34 and dependent claims 35-44 are drawn to methods for the prevention of gastric ulcers prior to the occurrence of gastric ulcer conditions in horses, i.e., in horses that have not previously had gastric ulcers. In contrast, FDA relates to prevention of reoccurrence of gastric ulcers in horses, and Papich relates to prevention of gastric ulcers in small animals that are predisposed to develop ulcers because of disease or drug therapy.

Therefore, the cited documents alone or in combination do not teach, suggest, or provide motivation for a skilled artisan to practice the presently claimed invention. Accordingly, reconsideration and withdrawal of the obviousness rejections are respectfully requested.

CONCLUSION

In view of the amendments and remarks made herewith, the application is in condition for allowance. Consideration and entry of this paper, favorable reconsideration of the application, reconsideration and withdrawal of the rejections of the application, and prompt issuance of a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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EXHIBIT 1

"Tufts Bulletin"

Horse Gastric Ulcer Bulletin from Tufts University School of Veterinary Medicine

(www.tufts.edu/vet/sports/ulcers.html)

TUFTS School of Veterinary Medicine

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Learn more about gastric ulcers

- **How does the horses's stomach work?**
- **What causes gastric ulceration in horses?**
- **What are NSAIDS and how do they cause gastric ulceration?**
- **What happens during the gastroscopic examination?**
- **How do we treat gastric ulcers?**

How does the horses's stomach work?

It is important to remember that horses are *herbivores*, meaning that they are true vegetarians. Consequently, the anatomy and physiology of their gastrointestinal system is much different from ours. It is also important to remember that horses have very small stomachs when you consider their size - only approximately 4 gallons at holding capacity. This, again, reflects the way that they would eat in the wild - very frequent small meals, so that the stomach is never stretched to full capacity. To start with, the horse's stomach is made up of two different parts. The primary difference between these two parts is that they have different types of cells lining them. Epithelium is a general term for the covering of any surface of the body, and it consists of many cells tightly joined to each other. The first type of epithelium encountered in the stomach is *stratified squamous epithelium*, after which a *glandular epithelium* is found. A distinct margin, called the *margo plicatus*, separates the two. Insert figure 1 - stomach anatomy The glandular epithelium, as its name suggests, contains many glands that produce gastric secretions. The squamous epithelium contains no glands, and merely serves to contain food, without aiding in any chemical digestion. The purpose of the stomach is to help in the long process of digesting food. In order to do this, the stomach must not only mix food, but produce secretions that help to break down food. Two digestive factors, *hydrochloric acid* (gastric acid) and *pepsin*, are produced in the glandular portion of the stomach. Both hydrochloric acid and pepsin begin the digestive process in the stomach before food reaches the small intestine. The glandular portion of the stomach also secretes factors that help to protect the stomach. One of these, a *mucus-bicarbonate layer* serves to protect the stomach lining both by preventing acid from physical contact with the stomach surface, and by buffering gastric acid at the level of the stomach lining .

This mucous-bicarbonate layer protects only the glandular portion of the stomach, and not the squamous portion. Other protective factors include

prostaglandin E, which causes increased blood flow in the stomach lining, increased secretion of the mucus-bicarbonate layer, and also causes decreases in hydrochloric acid production various growth factors. Unlike humans, horses produce gastric acid continually, regardless of whether they are eating regularly. If horses do not eat, then their stomachs become more and more acidic because acid production cannot be 'turned-off'. The squamous portion of the stomach is at the greatest risk from increased acid production, because it does not benefit from all the protective factors that the glandular portion of the stomach enjoys.

What causes gastric ulceration in horses?

Gastric ulceration in horses occurs when acid production overwhelms the protective factors. Although there is a clearly established bacterial cause of gastric ulceration in humans, we haven't been able to find a similar connection in horses. Rather, it seems that any situation that can allow acid to overwhelm the stomach's protective mechanicsms, such as infrequent, low-roughage feeding that leaves the stomach empty the majority of the time, can provide a window of opportunity for gastric acid to erode the stomach lining. With sport horses, intensive training, tends to go hand-in-hand with infrequent turnout and low-roughage, high-concentrate feeding. If we add to this chronic use of NSAIDs (non-steroidal anti-inflammatory drugs), we have a recipe for ulcer disaster!

What are NSAIDS and how do they cause gastric ulceration?

Common NSAIDs include phenylbutazone ('bute') and flunixin meglumine (Banamine™). They act by interrupting the production of *prostaglandins*, which are a diverse family of molecules with extremely diverse effects. The most familiar action of NSAIDs is that by blocking the production of prostaglandins, they help to decrease fevers, aches, and pains. One particular prostaglandin, called *PgE2*, plays an important role in preventing gastric ulceration. PgE2 does this by decreasing gastric acid production as well as by increasing blood flow to the gastric epithelium. Unfortunately, the NSAIDs that we commonly use to decrease fevers, aches, and pains also blocks normal blood flow to the stomach.. The results are multiple - the horse's stomach becomes more acidic, and this contributes to the development of gastric ulceration. Normal blood flow is necessary to healing, and so disruption of normal blood flow leads to a double whammy - not only does the horse develop gastric ulcers, but he also can't heal them very well. It's a vicious cycle.

What happens during the gastroscopic examination?

If, after extensive examination, we decide that the medical history and physical examination findings are very suggestive of gastric ulceration, the definitive way to diagnose gastric ulceration is with a very long

endoscope, known as a *gastroscope*. This allows us to place a camera inside the horse's stomach, and thus get a close-up view of the stomach lining. The type of endoscope that is commonly used to look at a horse's upper airways simply won't do - it isn't long enough. In order to visualize the adult horses stomach, an endoscope that is at least 220 cm long is necessary. That translates to 6.9 feet! In order to obtain a good view of the stomach, it is important for the stomach to be empty. That's why we'll usually ask you to keep your horse from eating for 18-24 hours before the gastroscopic examination. Your horse will still be able to drink during this time.

In order to do a gastroscopic examination, we must pass the scope through the nostrils, into the *pharynx*(area just before the *esophagus*, or swallowing tube), and then into the esophagus, and, finally, into the stomach. Although gastroscopy isn't painful to the horse, most horses do resent anything being passed through the nostrils. The anxiety can be diminished considerably by giving the horse a tranquilizer - usually xylazine or a combination of xylazine and another drug. Long 'scopes' with the ability to see all the way into the stomach are extremely expensive, and we'd rather keep your horse from chewing on it in case it doubles up and goes back into the mouth (yes, this has happened!). For this reason, usually a short plastic tube (similar to, but much shorter than the tube that is used for deworming your horse), is first passed through the horse's nose and into the esophagus, and then the scope is passed through that shorter tube.

- Gastroscopy itself doesn't take very long - only approximately 15-20 minutes. Because the stomach is a collapsible organ, it must often be pumped up with air during the examination so that every bit of the surface can be seen.
- Typical findings include areas of the stomach that are eroded, thinning, bleeding, or have abnormal amounts of scar tissue. Insert figures 3 (gastric ulcers at *post mortem*) and 4 (gastric ulcers seen with a gastroscope)
- After the gastroscopic examination is finished, all the air will be let out of your horse's stomach to avoid colic. Then, your horse will still be kept off any food until he seems to have fully woken from the tranquilizer.

How do we treat gastric ulcers?

The goal of treatment is to decrease the level of acidity in the stomach in order to allow the horse's natural healing processes to mend the ulcers. There are several ways to achieve this goal: all of them center around addressing the situation that allowed your horse to develop gastric ulceration in the first place. The way that you and your veterinarian choose to treat gastric ulceration will usually depend on your schedule as well as your ability to change your horse's environment.

Drugs:
Most horses do require some drug therapy in order to successfully treat gastric ulcers. Drugs designed to treat gastric ulcers may 1) decrease

the amount of acid produced by the stomach, 2) physically coat the stomach to prevent the acid from wreaking havoc, or 3) buffer the acid in the stomach.

Drugs that decrease the amount of acid produced by the stomach:

1. H-2 blockers:
   These drugs block histamine, one of the factors that stimulates acid production. They reduce the signals to the acid-producing cells, so that they slow down their rate of acid production. Drugs that fall into this category include cimetidine, ranitidine, and famotidine. All of these are available as over-the-counter drugs for humans, albeit in much smaller concentrations than are suitable for a horse! Most of them must be given three times a day for them to work properly.
2. Proton pump inhibitors:
   Proton, or hydrogen pumps, are the mechanism by which acid is actually produced by the cells. Acidity is merely a reflection of the amount of hydrogen ions, or protons that are in a fluid. If you prevent the pumps from working, then the acid level will decrease dramatically. Gastroguard® is a proton pump inhibitor that is now on the market for horses. One of the nice features of this drug is that it is only given once a day.

Drugs that block acid:
The most commonly used drug that blocks acid from getting access to the stomach lining is sucralfate. Sucralfate, however, is best for helping to heal ulcers in the glandular mucosa, and most adult horses have ulcers in the squamous mucosa. For this reason, it is not suitable for use on its own in treating gastric ulcers in adult horses.

Drugs that buffer acid:
Antacids are commonly used in humans, and some veterinarians advocate using them in horses. Antacids can buffer an adult horse's stomach, however, the effect lasts for less than an hour, and very large volumes (over 1/3rd of a pint) must be used.

Feeding and environmental changes:
It is difficult to impossible to fully heal gastric ulcers using drugs alone. The most important thing we can do to heal ulcers is to recognize that horses need to live like horses! In the wild, horses do not have two, or three, or even ten meals a day - they eat small amounts of roughage all the time. If we fed horses the way they are meant to be fed, we probably wouldn't ever have to treat ulcers. The drugs may vastly improve the clinical signs, but many veterinarians report that the ulcers themselves still persist. In order to have full resolution of the gastric ulcers, it is important to give the horse as much 'down time' as possible. In the best of all possible worlds, this would mean pasture turnout for 24 hours a day. Your horse should also be given free choice hay, so that he always has something in his stomach. If possible, grain should be avoided. If your horse needs the extra calories, they can be supplemented with many small meals and the addition of high calorie vegetable oil to his food.

It is important to remember that although your horse's signs may abate within the first week of treatment, the ulcers do not heal without at least three weeks of drug therapy and changes in environment and feeding. It is very important to follow your veterinarians recommendations for the frequency and length of treatment, as well. For instance, your horse may feel a lot better after he is given a low dose of cimetidine twice a day, instead of the recommended high dose three times a day. However, at the end of three weeks, your horse will likely still have gastric ulcers.

If it is at all possible, you should have a re-check gastroscopy performed 3-4 weeks after you start treatment. In this way, you will have hard evidence of how well the ulcers are healing. You will be able to make a more intelligent and informed decision about how long, if at all, you should continue treatment.

Back to Ask the Doctor

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EXHIBIT 2

Canine Nutrition

(www.knowbetterdogfood.com/dogcare/health/nutrition.php)

Dog Nutrition - Selected information compiled by Know Better Dog Food

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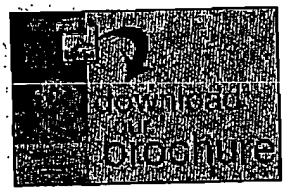

Feeding for Optimum Health and Longevity

Canine digestive system anatomy and physiology is, mainly, that of a carnivore, the most distinct characteristic being the voluminous stomach and shorter intestinal length indicative of a carnivore to aid in rapid digestion of raw meat. The entire anatomy of the dog is adapted for a raw meat diet. A natural diet (raw meat and predigested plant material) are the foods best suited to the dog. Although domestication has changed their external appearance, their nutritional needs have not changed from those of their wild ancestors.

This brings us to the undisputable conclusion that there are many undesirable aspects of the commercial pet food industry. Among the many reasons to avoid feeding commercial pet food, two predominate: All commercial pet foods are heat processed, thereby effectively destroying the natural enzymes present in the ingredients and the fact that the vast majority of pet foods are made with animal parts that have been determined unfit for human consumption and have been treated with chemicals to ensure they do not get back into the human food chain. Enzymes are an essential aid in proper digestion of foods and supply the body with the energy needed for such activities as the formation and elimination of urea and carbon dioxide and other toxins from the kidneys, lungs, colon, liver, spleen, and skin created during the process of metabolism. Ingesting quantities of contaminated and indigestible animal parts and plant material (and usually combined with chemical preservatives and other additives) on a daily basis cannot be considered conducive to good health. Studying carnivore anatomy, physiology, and eating habits shows us that we are doing our domestic friends a great disservice by not feeding them the way nature intended.

Carnivore Anatomy and Physiology

Carnivores have a simple hinge jaw that works in a scissoring/slicing fashion rather than the rotational fashion of the herbivore and therefore do not chew and cannot grind grains, vegetables and fruit. Their saliva is acidic, of which they produce large amounts to lubricate the food bolus and the esophagus for transport to the stomach, but do not produce the carbohydrate digesting salivary enzymes herbivores do – it is not necessary for the food to remain in the mouth and be well-mixed with saliva as it is with the herbivore.

The carnivore stomach has a voluminous capacity and plays the largest role in the digestive process (it makes up 60-70 percent of the total volume of the digestive tract, the herbivore less than 30 percent) and is where the majority of protein, i.e., meat, digestion takes place. Food stays in th stomach for up to ight hours, as opposed to the herbivore's 2-3 hours. This nsur s the meat is well broken down before entering the intestinal tract where toxins released by putrefying meat could be absorbed; it secretes large amounts of hydrochloric acid (t n times mor than the herbivore) creating the highly acidic stomach nvironment necessary for digesting meat protein and killing any dangerous bacteria that may have been ingested. The carnivore small intestine is short (3-6 times body length) compared to the

herbivore at 10-12 times the body length.

Carnivores have a poorly developed sense of tast – smell is much more important to them (the dog has 1,700 taste buds to people's 9,000)

The carnivore liver is large (the dog has the largest liver of all animals) and produces uricase, an enzyme that breaks down uric acid. The carnivore liver is capable of eliminating 10-15 times more uric acid than the liver of the herbivore (meat digestion releases large amounts of uric acid).

The carnivore, in nature, sleeps an average of 18-21 out of 24 hours in a day. The herbivore sleeps from 1-3 hours a day, eating (grazing) on a continuous basis for the other 21-23 hours.

Carnivore Eating Habits

Carnivores, including dogs, gorge themselves on their prey, swallowing large chunks of food that we, as humans, would choke on; usually the organs are eaten first, followed by the stomach and intestines. This is nature's way of ensuring a balanced diet by supplying a source of semi-digested carbohydrates and plant material for intestinal flora and important nutrients and unsaturated fats needed by the carnivore, as well as the nutrients stored in the organs that are not found in the bones and muscle tissue. They will eat the whol carcass – skin, hair and bones included – the extremely acidic stomach environment can digest bones and skin, the hair acts as a natural fiber, bulks up the stool and protects the intestinal walls from sharp objects such as fragments of bone. (Note: commercial foods do NOT promote an acidic stomach environment). After gorging they will then sleep off and on for an extended period of time while digesting their meal. Gorging ensures that the stomach gets fully exercised, strengthened and toned the way it is meant for proper functioning.

Fasting is an important part of carnivore behavior, allowing for complete digestion of the raw meat protein while allowing the stomach to be cleaned and completely emptied regularly.

The Importance of a Raw Meat Diet

Raw meat helps to maintain the acidic environment necessary for its digestion and absorption of calcium from bones; the acidic environment simulates the pancreas to produce its digestive enzymes – this maintains pancreatic health and prevents atrophy of this important organ; the strong digestive secretions allow very few parasites to get past the stomach. It is important to note that cereals, i.e., grains, are alkaline forming – this means that commercial pet foods, which are cereal based, do not nurture an acidic stomach environment.

Cooking meat artificially semi-digests it instead of allowing the stomach, intestines, and digestive enzymes being allowed to do so. This leaves these organs improperly exercised and over a period of time their ability to function naturally and to cope with the work they were meant to do is compromised, opening the door for the development of chronic health concerns.

Cooking destroys many important nutrients and also the enzymes necessary for all of the body's physiological functions. The body does manufacture enzymes, but in the absence of the enzymes obtained from raw food, the body overworks its natural supply. This creates a strain on its enzyme reserve which can impair and stress the functioning of all the major organ systems of the body – leading to a state if disharmony and disease. Cooking causes the amino acid chain found in meat protein to coagulate and become useless and/or toxic to the body, incr asing its burden to detoxify.

Cooking also depletes the vital high water cont nt of natural foods. Heating extracts the

natural water and dries and concentrates the food; water is critical for all functions, as well as storing the water-soluble vitamins required by the body.

Cooked food passes through the digestive trace more slowly than raw food, tending to putrefy and throw toxins back into the bloodstream; prolonged intestinal toxemia may manifest itself in a myriad of disease symptoms, including allergies and arthritis.

A raw meat diet prevents the formation of plaque on the teeth and the high acidity of the oral cavity destroys any harmful bacteria before they have a chance to contribute to periodontal disease. Periodontal disease has become almost epidemic in our dogs today and plays a major role in the creation of ill health in our pets. Note: carnivores need predominantly a raw meat diet, but also require some raw plant material in a predigested form (as found in the stomach and intestines of their herbivore prey).

Conclusion

The complex metabolic processes of the body must be fueled in a supporting and vitalizing fashion, the way nature intended, in order for good health and a disease-free state to be maintained. A natural, chemical-free diet nurtures optimum health, and as concerned and loving pet guardians we owe it to them to take a serious look at what and how we are currently feeding them.

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